A time of enlightenment: straightforward identification of protein modifications

We have known for decades that protein modifications are key to understanding protein function, and regulation of protein function. However, we also know that we have not yet assembled a complete picture of the modifications that occur on the proteins that we analyse. This current lack of detailed information at the modification level is principally a bioinformatics problem.

Indeed, our instruments are quite capable of recording identifiable fragmentation spectra of modified peptides, but our search engines are incapable of reliably identifying these modified peptides. This bioinformatics problem has two sides: first, it stems from the combinatorial explosion that occurs when all possible modifications (and all single-amino acid mutations) are considered, and second, it stems from poor use of the information in spectra by our current search engines.

We have therefore developed a new tool called ionbot, which solves both problems, and which offers an unprecedented view on the modified proteome. The results are highly interesting, and dramatically broaden our view on what happens to our samples in vivo as well as in vitro, revealing both biological modifications and artefactual modifications introduced during sample processing.

For a long time, it has been clear that the proteome is much more complex than a collection of identified proteins and their relative abundances, and that protein modifications play an outsize role in understanding biology. As a field, we therefore have already made considerable progress in our understanding of a small subset of modifications with high relevance. But new tools such as our ionbot search engine will now cause a dramatic expansion of our view on the proteome, and will certainly deliver a plethora of new leads for further research into the delicate fine-tuning of life itself, by revealing the modifications that drive the appearance, the localisation, the function, and ultimately, the fate of the proteins that make life happen.